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Neuroethics Questions to Guide Ethical Research in the International Brain Initiatives

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Increasingly, national governments across the globe are prioritizing investments in neuroscience. Currently, seven active or in-development national-level brain research initiatives exist, spanning four continents. Engaging with the underlying values and ethical concerns that drive brain research across cultural and continental divides is critical to future research. Culture influences what kinds of science are supported and where science can be conducted through ethical frameworks and evaluations of risk. Neuroscientists and philosophers alike have found themselves together encountering perennial questions; these questions are engaged by the field of neuroethics, related to understanding of the nature of the self and identity, the existence and meaning of free will, defining the role of reason in human behavior, and more. With this Perspective article, we aim to prioritize and advance to the foreground a list of neuroethics questions for neuroscientists operating in the context of these international brain initiatives.

Background

Neuroscience has become a national priority for governments across the globe as evidenced by seven active or emerging national-level brain research initiatives (Grillner et al., 2016; Huang and Luo, 2015): Australia (Richards and Committee, 2016), Canada (https://www.canadianbrain.ca/), China (Poo et al., 2016), the EU (Amunts et al., 2016), Japan (Okano et al., 2016), Korea (Jeong et al., 2016), and the US (Jorgenson et al., 2015) (Table 1; Figure 1). These initiatives collectively represent a proposed investment of over $US 7 billion. Such an investment reflects the importance of the potential afforded by a deeper understanding of the brain and recognition that neuroscience can dramatically shift the landscape of our lives.

Advances in neuroscience continue to reveal and pose unprecedented ethical issues. These issues range from general concerns about societal goals and values to more specific questions about desirable outcomes for neuroscience research (PCSBI, 2014; Rose, 2014), to perennial philosophical questions related to the nature of understanding the self and identity, whether or not free will exists, the nature of emotion, the role of reason in human behavior, and memory (Evers et al., 2017). The expansive implications of neuroscience in defining humanity have contributed to the status of neuroscience as a national-level funding priority across the globe.

Neuroethics complements the discipline of neuroscience by providing a robust set of tools for informing the design and conduct of biomedical research as well as analyzing how neuroscience findings impact society and may transform social institutions. Neuroethics can be understood as a mutually informing collaborator that can advance the field of neuroscience by anticipating the near-term to far-reaching—often unexpected–implications of new technologies, findings about the brain that result from examining the brain, and the implementation of these technologies. To the neuroscience community, neuroethics provides a critical lens for reimagining, framing, and often focusing the questions and potential impact of specific research projects (Box 1).

Thus, the priority of making neuroethics an integral part of the neuroscientific enterprise has moved beyond the academy and has registered at the highest levels of governments (Table 1). For example, the European Union's Human Brain Project (HBP) from its inception has had structural and financial resources dedicated to projects on the attendant philosophical and ethical issues of neuroscience research (Amunts et al., 2016; Evers, 2016). The Ethics and Society subproject of the HBP research core publishes opinions about relevant HBP-related ethical issues and one of the research groups under this subproject is dedicated to neuroethical and philosophical questions (https://www.humanbrainproject.eu/en/social-ethical-reflective/neuroethics-and-philosophy/). The HBP also has an Ethics Rapporteur system wherein researchers from each of the twelve research subprojects routinely discuss ethical issues with the HBP Ethics Advisory Board and with Ethics

Table 1. The International Brain Initiatives

Project	Goals and Potential Impact	Neuroethics Component	Total Budget for Duration of Project (US Dollars)	Duration
Australian Brain Initiative (https://www.brainalliance.org.au/)	Goals: "…optimizing and restoring brain function, developing advanced neural interfaces, understanding the neural basis of learning across the lifespan, and developing new insights for brain-inspired computing" (Richards and Committee, 2016, p. 599). Potential Impact: create advanced industries in neurotechnology; develop treatments for debilitating brain disorders; produce high-impact interdisciplinary collaborations that will increase understanding of the brain.	neuroethics committee part of initial ABI design	500 million over 5 years	project is in development, estimated 5 years
Canadian Brain Research Strategy (https://www.canadianbrain.ca/)	Goal: understanding how the brain learns, remembers, and adapts. Potential Impact: develop and maintain a large-scale Canadian network in Open Science and Data Sharing.	neuroethicist on committee	TBD	project is in development
China Brain Project	Goal: understanding cognitive disorders with a focus on autism, depression, and Alzheimer's disease; child and adolescent development of intelligence; brain inspired machine intelligence and intelligent socially interactive robots. Potential Impact: basic understanding of neural circuit mechanism underlying higher cognitive functions; molecular, imaging, and functional markers for early diagnosis of brain disorders; physiological and physical approaches for early intervention; new generation of brain-inspired artificial neural networks, computing devices, and intelligent robots (Poo et al., 2016).	TBD	TBD; estimated 1 billion	Project is in development. Estimated 15 years, including 5 year startup period (Normile, 2018).
EU Human Brain Project (https://www.humanbrainproject.eu/en/about/overview/)	Goal: "creating a research infrastructure to advance neuroinformatics, brain simulation, high performance analytics and computing, medical informatics, neuromorphic computing, and neurorobotics" (Amunts et al., 2016). Potential Impact: neuromorphic and neurorobotic technologies; supercomputing technologies for brain simulation, robot, and autonomous systems control and other data intensive applications; personalized medicine for neurology and psychiatry.	Research Project (SP12) dedicated to neuroethics from 2013; includes Ethics Management as part of the directorate, an Ethics and Society Subproject (SP12), an Ethics Rapporteur Program, and an external Ethics Advisory Board and Ombudsperson	1.2 billion; 4% of budget for ethics	2013–2023
Japan Brain/MINDS (https://brainminds.jp/en/central/mission)	Goals: "…developing the common marmoset as a model animal for neuroscience, the project aims to build a multiscale marmoset brain map, develop new technologies for experimentalists, create transgenic lines for brain disease modeling, and integrate translational findings from the clinical biomarker landscape" (Okano et al., 2016, p. 582). Potential Impact: high-resolution, wide-field, deep, fast, and long imaging techniques for brain structures and functions; techniques for controlling neural activity; determine causal relationships between the structural/functional damage of neuronal circuits and disease phenotypes; eventually develop innovative therapeutic interventions.	a neuroethics group in Strategic Research Program for Brain Sciences (SRPBS) has supported neuroethics issues on Brain/MINDS	300 million	2014–2023

(*Continued on next page*)

Table 1. ***Continued***

Project	Goals and Potential Impact	Neuroethics Component	Total Budget for Duration of Project (US Dollars)	Duration
Korea Brain Initiative	Goal: "mapping of a functional connectome with searchable, multi-dimensional, and information-integrated features. The project also includes the development of novel technologies and neuro-tools for integrated brain mapping. Beyond the scientific goals this grand endeavor will ultimately have socioeconomic ramifications that not only facilitate global collaboration in the neuroscience community, but also develop various brain science-related industrial and medical innovations" (Jeong et al., 2016, p. 607). Potential Impact: brain mapping platforms and high-throughput technologies to unravel the structural and the mechanistic bases of higher brain functions, such as decision-making, attention, and memory to develop brain-inspired artificial intelligence systems; precision medicine-based approaches to develop therapeutic interventions of neurological disorders (Jeong et al., 2016).	neuroethics committee part of initial KBI design	350 million	2016–2026
US BRAIN Initiative (http://www.braininitiative.org/alliance/)	Goals: accelerate the development and application of new technologies that will enable researchers to produce dynamic pictures of how individual brain cells and complex neural circuits interact at the speed of thought. Potential Impact: complete cell census of mouse and, later, human brain; technologies to precisely modulate activity of specific neural circuits; devices for *in vivo* high-density intracellular recording; technologies that expand our ability to monitor activity non-invasively in the human brain; link brain activity to behavior; data analysis tools to help understand the biological basis of mental processes.	President's Commission for the Study of Bioethical Issues focus on neuroscience in 2013–2015; Neuroethics Working Group formed in 2016; Neuroethics Research Grants available in 2017 and 2018; Neuroethics Subgroup of the Advisory Committee to the NIH Director, 2018–2019	budget projected to be 6 billion; neuroethics grants in 2017–2018, 2 million/year	2013–2025

Adapted from OECD (2017) Table 2.1.

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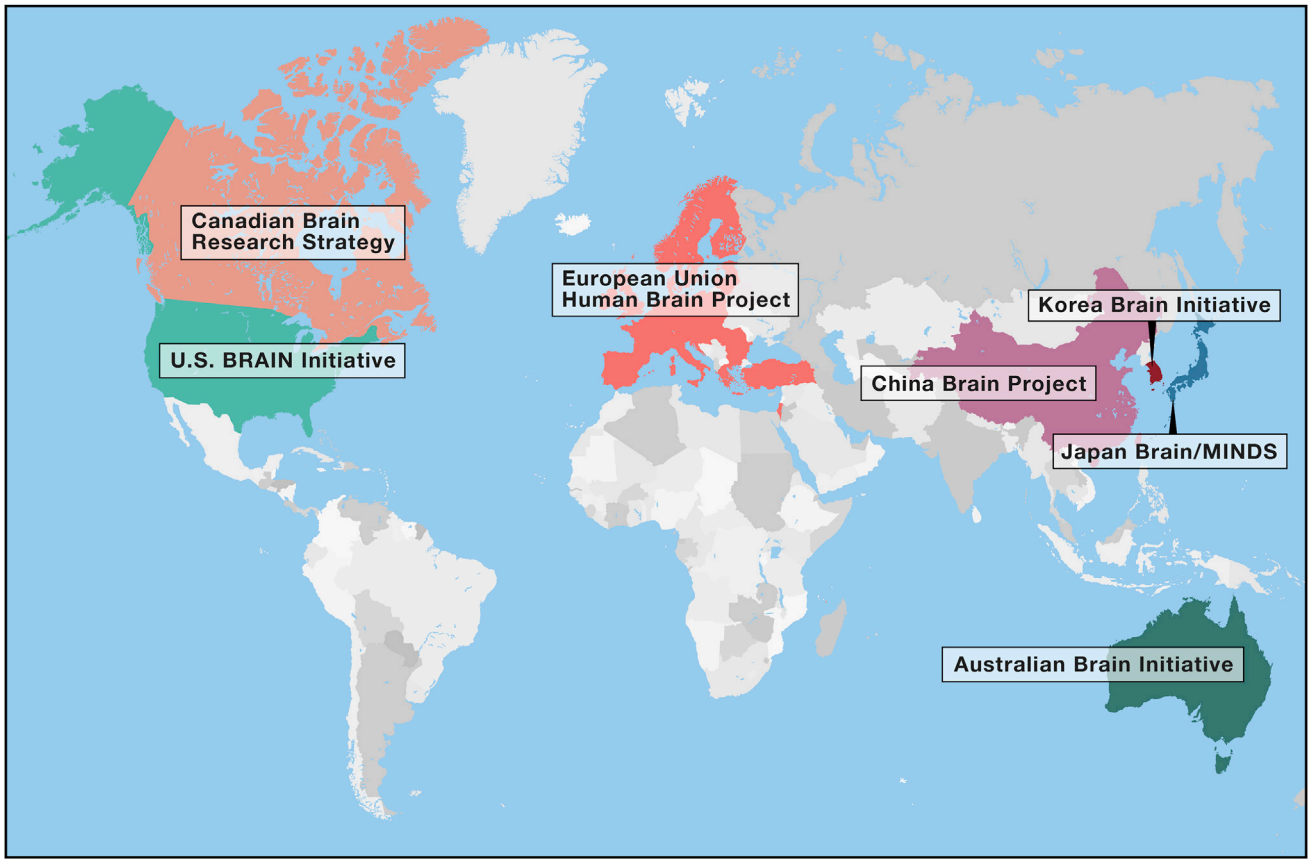

Figure 1. The International Brain Initiatives
Adapted from Yuste and Bargmann (2017) Figure 1.

Support. The Australian Brain Alliance (Richards and Committee, 2016), Canadian Brain Research Strategy, and Korea Brain Initiative (J. Illes and S.-J.J., personal communication) have incorporated neuroethics and neuroethicists into the design of their emerging and recently launched national brain research programs. In China, scientists are working with the Chinese government to incorporate a neuroethics committee into the China Brain Project. The United States Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative (https://braininitiative.nih.gov/index.htm), included tasking the Presidential Commission for the Study of Bioethical Issues with exploring the attendant ethical issues of neuroscience research writ large. Recognizing that the rapid pace of technology often supersedes the ways scientists and engineers understand the social implications of their work (Check, 2007; Heffernan, 2010), the team created two reports emphasizing that neuroethics should be a requisite part of all neuroscience research (PCSBI, 2014, 2015) and an integral part of training the next generation of neuroscientists. These reports shaped the implementation of the BRAIN Initiative neuroethics program, including offering large-scale grants for neuroethics research (https://www.braininitiative.nih.gov/about/neuroethics.htm). The BRAIN Initiative has established a Neuroethics Working Group and has program officers managing a neuroethics grant portfolio. A recently formed BRAIN Working Group of the Advisory Committee to the NIH Director, tasked with evaluating the blueprint for BRAIN (BRAIN 2025: https://www.braininitiative.nih.gov/2025/), also has included a Neuroethics Subgroup to develop a Neuroethics Roadmap for the Initiative.

Good neuroethical practice should also lead to engaging with the underlying values and ethical concerns that drive brain research across cultures and continents. Ultimately, cultural values influence not only how science is done, but also how the science might be adopted and integrated in societal practice. The consequences of cultural misunderstandings are far from trivial for the scientific enterprise. Gaps in understanding lead to missed opportunities for collaboration and advancement toward future discoveries, limit the ability to broadly share results and thereby reap the benefits of neuroscience findings, and ultimately result in a failure to recognize the short- and long-term potential and risks of neuroscience research. These cultural differences exist between national entities, within defined societies, and also among individual researchers and practitioners. And yet in the 15-year history of the field of neuroethics, there has been little work engaging cultural perspectives, and when different cultural perspectives are presented, they are done so in isolation without comparison and analysis across cultures. Culturally informed and aware neuroethical inquiry, understood as a process of intentional perspective-taking, can be useful in

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Box 1. Scholarly Traditions for Analyzing the Social and Ethical Implications of Neuroscience

Over the past few years, a number of approaches have focused on the social and ethical implications raised by neuroscientific research (Eric and Matthew, 2017). One approach, critical neuroscience, calls for a more reflective neuroscientific practice that calls largely upon the social sciences to examine the potential and limitations of the questions and methodologies of neuroscience (Choudhury et al., 2009). A second approach is neuroethics that attempts to complement the discipline of neuroscience by providing a robust set of ethical and philosophical tools for analyzing how research is designed and conducted as well as how neuroscience findings impact individuals and the societies they live in. Thus, neuroethics can be understood as a mutually informing collaborator that advances the field of neuroscience by identifying, critically addressing, and illustrating the near-term to far-reaching—often unexpected—implications of the new technologies, findings about the brain that result from examining the brain, and the implementation of new technologies (Salles and Evers, 2017).

This relatively new field of neuroethics, focused on neuroscience and its design, methods, conduct, and the impact of its products on society, has sometimes been accused of not offering much from a critical perspective and of overstating the positive impact of neuroscientific findings (Brosnan, 2011; De Vries, 2005; Racine, 2010). At its best, far from being an uncritical advocate of neuroscience, neuroethics can remain constructively critically aware, providing a lens for reimagining the questions and potential impact of specific research projects.

Still, such critique has prompted some neuroethics scholars to argue for a "fundamental neuroethics," a term employed by the philosophy research group of the HBP, which aims to delve into deep conceptual philosophy, to explore *how* scientific inquiry can be used to address a number of fundamental philosophical questions (Evers et al., 2017) and how such questions might be explored in the context of responsible research innovation (RRI) (Salles et al., 2018). RRI is a normative framework that has dominated EU policy and governance that generally encourages stakeholder involvement to collectively discuss how best to advance societal goals through technology innovation. For additional explanation of normative frameworks on evaluating neurotechnology and society, including RRI, please see section 5, p. 27 of the 2017 OECD report (OECD, 2017).

generating novel questions and thereby driving more fruitful and ethical global science. However, particular care is needed in assessing cultural perspectives as one risks reinforcing ill-informed stereotypes rather than thoughtful engagement. Our emphasis on perspective-taking here encourages reflection and inquiry of the values and philosophical traditions within and across national settings.

Beyond a cursory mention in reports and guidelines by independent groups (Goldschmidt and Renn, 2006; Yuste et al., 2017), no national project has explicitly discussed cultural perspectives when engaging these neuroethics and neuroscience questions. Furthermore, no report has addressed what engaging neuroscience with a cross-cultural lens might look like, although recent reports from the Organization for Economic Co-operation and Development (OECD) make special note of the need for cross-cultural evaluations in technology development (Garden and Winickoff, 2018; OECD, 2017). A culturally informed analysis is urgently needed given the global collaborative nature of neuroscience research and the recent commitment to the formation of the International Brain Initiative, a collaborative entity comprised of all existing national-level brain projects (https://www.brainalliance.org.au/learn/media-releases/worlds-brain-initiatives-move-forward-together/). With this paper, we aim to establish a list of neuroethics questions for neuroscientists (NeQNs) (Box 2) in general and, in particular, those operating in the context of these global brain projects.

Culturally Informed and Aware Neuroethics: An Integrated Approach?

While there are numerous philosophical approaches that would be useful in addressing the concerns of neuroscience (Evers et al., 2017), mainstream Western bioethics, which has emerged in response to Western biomedicine's largely non-explicit individualistic orientation, has dominated neuroethics discussions to date (Burton, 2007; Chattopadhyay and De Vries, 2008, 2013). Therefore, the more prevalent neuroethical approaches may not be fully capturing the richness of the relevant issues for neuroethical inquiry across the sites of national brain projects. It is necessary to ask how the prevalent Western approach—largely conceived as a matter of obligations to individual rights bearers rather than the often more globally prevalent communitarian concerns—applies to the moral aspirations and requirements of a broader global community, a community characterized by diverse values and beliefs. Through culturally informed neuroethics, we can gain a stronger acknowledgment and understanding of cultural values—values that can both be geographically specific, but are also more likely represented on a spectrum across geographic regions and peoples (Stevenson et al., 2016). We can also begin to uncover the extent to which some of those cultural values are morally relevant, should be upheld, or can be challenged. Fundamentally, cultural values impact the neuroscientific agenda, what questions should be considered to be within the purview of brain studies, and how neuroscience findings are understood.

Central to typical neuroethics discourse is brain exceptionalism: the belief that the brain, distinct from any other organ, is foundational to human identity because it is the locus of fundamental human elements such as personality, desires, hopes, fears, memories, and free will. Neuroscience has become a national research priority across the globe not only because of the global burden of brain diseases, but also because researchers and funders have set as among their goals "unlocking the elusive secrets of the human brain" (Martin and Chun, 2016, p. 573) and deeper understanding of "human feelings and behavior" (Okano et al., 2015, p. 2), and ultimately our essential human-ness. It is unclear, however, the degree to which these constructions of

Box 2. Neuroethics Questions to Guide Ethical Research in the International Brain Initiatives

Q1. WHAT IS THE POTENTIAL IMPACT OF A MODEL OR NEUROSCIENTIFIC ACCOUNT OF DISEASE ON INDIVIDUALS, COMMUNITIES, AND SOCIETY?

1a. What are the possible unintended consequences of neuroscience research on social stigma and self-stigma?
1b. Is it possible that social or cultural bias has been introduced in research design or in the interpretation of scientific results?

Q2. WHAT ARE THE ETHICAL STANDARDS OF BIOLOGICAL MATERIAL AND DATA COLLECTION AND HOW DO LOCAL STANDARDS COMPARE TO THOSE OF GLOBAL COLLABORATORS?

2a. How can human brain data (e.g. images, neural recordings, etc.), and the privacy of participants from whom data is acquired, be protected in case of immediate or legacy use beyond the experiment?
2b. Should special regard be given to the brain tissue and its donors due to the origin of the tissue and its past?

Q3. WHAT IS THE MORAL SIGNIFICANCE OF NEURAL SYSTEMS THAT ARE UNDER DEVELOPMENT IN NEUROSCIENCE RESEARCH LABORATORIES?

3a. What are the requisite or minimum features of *engineered* neural circuitry required to generate a concern about moral significance?
3b. Are the ethical standards for research conduct adequate and appropriate for the evolving methodologies and brain models?

Q4. HOW COULD BRAIN INTERVENTIONS IMPACT OR REDUCE AUTONOMY?

4a. What measures can be in place to ensure optimal autonomy and agency for participants/users?
4b. Who will have responsibility for effects (where responsibility has broad meaning encompassing legal, economic, and social contexts)?

Q5. IN WHICH CONTEXTS MIGHT A NEUROSCIENTIFIC TECHNOLOGY/INNOVATION BE USED OR DEPLOYED?

5a. Which applications might be considered misuse or best uses beyond the laboratory?
5b. Does this research raise different and unique equity concerns and, if so, have equitable access and benefit of stakeholders been considered?

the brain-body-mind relationship, or the identification of the brain with "who we are," are universally embraced in the communities where brain research projects are occurring (Descartes, 1985; Gillihan and Farah, 2005; Kitayama and Park, 2010; Nisbett and Miyamoto, 2005; Sakura, 2012; Vidal, 2009; Yang and Miller, 2015; Yu, 2009). For many cultures, the mind, brain, and body are inextricably linked, as typified by the Chinese and Japanese concept of or *xin* or *kokoro* (心), meaning mind-heart-spirit as inseparable features (Swanson, 2011; Yu, 2009). The same character is recognized as *maum* (마음) in Korean. A society's, including its scientists', interpretations of these relationships can greatly influence the choice of projects pursued and the way research is conducted, and delimit the ultimate applications of neurotechnologies. Cultural views on death or brain death are not universal (Asai et al., 2012; Yang and Miller, 2015), nor are views of the inviolability of life, as evinced by gene editing of human embryos first in China and subsequently in the UK and US (Liang et al., 2015). Cultural differences have had a marked impact on what is considered permissible in national funding for research. Nonhuman primate (NHP) research has now become a focus of some projects in East Asia (Okano et al., 2016; Poo et al., 2016), even while NHP moral status is increasingly debated in the West. The rapid development in the sciences, in East Asia in particular, and the not-so-gradual relocation of a number of high-stakes, scientific, and biomedical enterprises from the West to East Asia, have made it imperative to engage with the plurality of existing ethical standards in order to realize the full potential of a collaborative global scientific enterprise.

To be clear, the weight and responsibility of examining societal values and motivations, and of conducting ethical and culturally aware neuroscientific research, should not be placed on scientists alone. Best practices for ethical scientific endeavors can flourish only when mechanisms and supports exist that encourage or enable scientists to do so. This is especially true given the demands on and incentives for scientific researchers to pursue scientific activities that may not achieve the highest ethical standards. Wherever possible, incentives for best ethical practices should be built within grant structures and interdisciplinary work. The actors involved in providing such support include the government, funders, universities, companies, and the public.

In order to promote awareness and discussion of these matters, we now present neuroethics questions to guide neuroscience research in the international brain initiatives, or neuroethics questions for neuroscientists for short (NeQN). While many of these questions are best asked by individual researchers as they design their projects, reflection on the nature and import of these questions by institutions, grant agencies, and society at large is essential to ensuring that researchers are encouraged

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Box 3. About the Global Neuroethics Summit

In 2016 at the UN General Assembly meeting, representatives of each of the brain projects in development or already launched met to discuss the creation of an International Brain Initiative (IBI). In winter 2017, a formal declaration of intent to form the IBI was announced (https://www.brainalliance.org.au/learn/media-releases/worlds-brain-initiatives-move-forward-together/). In the same spirit, the Global Neuroethics Summit aimed to bring together the global neuroethics projects to discuss how to align neuroethics efforts with the first step being to engage in developing a set of cross-cultural neuroethics questions to accompany and to be integrated into research in these brain projects. We also were grateful for the case study model provided by a parallel meeting in 2016 called Our Brain, Ourselves, Our World (http://o3brain.org/).

We brought together leading neuroscientists, ethicists, policymakers, sociologists, and cross-cultural scholars associated with each of the national-level brain research projects to attend a 2-day Global Neuroethics Summit in Daegu, South Korea. We endeavored to generate a list of neuroethics questions for neuroscientists across these brain projects. Details about the program and attendees can be found at https://globalneuroethicssummit.com/. See Table S1 for question development process. The resultant questions (Box 2) are meant to be adaptable and informed by the cultural values and frameworks of each country, beyond traditionally Western philosophical values.

The goal of the summit was to have a conceptual investigation and challenge what we may typically assume we all know when we discuss common neuroethics topics.

This is a very different and deliberate approach from previous discussions on best practices and policies in neuroethics. For example, while we may all agree that privacy is important to protect and honor for those who participate in neuroscience research, we may not all have the same ideas on the values that inform why privacy is worth protecting, or on the concept of what privacy is. Our work was to unpack some of these assumptions and to embark on cross-cultural perspective-taking while avoiding the pitfalls of moral relativism (e.g., there's no moral standpoint we can agree upon) and moral imperialism (e.g., there's only one moral truth). We also were mindful to engage in helpful perspective-taking exercises to avoid oversimplifying or stereotyping specific groups, cultures, or individuals.

to ask these types of questions and are recognized when they do. Embedding these research questions within the design of future experiments can enrich future research findings and anticipate ethical roadblocks that have the potential to otherwise delay or halt projects.

Neuroethics Questions for Neuroscientists

In recognition of the importance of cultural perspective-taking, a group of experts gathered to generate a general list of neuroethics questions that could be addressed across all national-level brain initiatives. We intend this exercise to serve as a model and starting point (not the conclusion) for culturally informed neuroethics (Box 3; Table S1; on process and about the Global Neuroethics Summit). NeQNs are deliberately intended to be adaptable, nimble, and informed by the local cultural value frameworks of each country hosting a national-level brain project. We hope that these NEQNs will also have value to neuroscientists beyond the brain projects, but we utilize the contexts of the existing and emerging large-scale national brain projects in Australia, Canada, China, the EU, Japan, Korea, and the US to illustrate the importance of this type of ethical inquiry in neuroscience. Because many of these projects represent countries in East Asia, we illustrate neuroethics questions through the underrepresented ethical frameworks found in East Asia such a Buddhism and Confucianism. Foregrounding these questions is intended to empower neuroscience researchers and their necessary partners to integrate and address these considerations within their research.

Q1. What is the potential impact of a model or neuroscientific account of disease on individuals, communities, and society?

As we continually learn more about the role of the brain and its functions, neurobiological data are being used in both expected and unexpected ways. To illustrate, such data have been taken to be exculpatory in legal proceedings (Aspinwall et al., 2012). While the influence of medical models of mental health may increase help-seeking (Chen and Mak, 2008), research has also shown that neurobiological accounts may increase the stigma visited on individuals with certain mental illnesses, such as schizophrenia and alcohol dependence (Pescosolido et al., 2010). Neurobiological accounts may have unpredictable effects on the self-understanding and self-efficacy of individuals with some mental illnesses (Kvaale et al., 2013). For example, identifying the neurobiological mechanisms of mental illnesses may reduce some of the self-blame associated with a disease, but may also reduce a person's belief in their ability to control their symptoms or to overcome their illness.

Many national brain projects are seeking improved or new predictive testing for brain-related conditions such as autism spectrum disorders and Alzheimer's disease. These early assessment tools may provide an opportunity to intervene early and slow the progression of disease (Arias et al., 2018). Many of these tools involve portable, relatively inexpensive, and user-friendly devices such as eyetracking with the aim of enabling wider universal use and access. However, predicting future brain health may impact not only what disease people believe they may develop, but also who they think they might become (Sarrett and Rommelfanger, 2015). Similarly, other techniques that national brain projects seek to develop would establish typical or "normal" maps of brain circuitry or activity. These mapping activities potentially mark individuals as being different from the norm, which may identify them as deviant and treated differently by their communities. As with mental illness, these diseases transform not only the relationship of individuals with their environments, but also their relationships with family members and

loved ones. For example, in cultures where philosophical and moral traditions such as Buddhism and Confucianism are embraced (Chen and Fan, 2010), there is a tendency to conceive of the self as irreducibly relational. In these contexts one's relationships reinforce a sense of identity. "Who I am" therefore is fundamentally a matter of being with and interacting with others. While family and friends are often impacted by the patient's illness regardless of culture, the experience is qualitatively different and deeper in traditions that conceive of self as relational. When prediction technology suggests a patient may have a brain disorder or disease, this not only deeply impacts the individual, but also strongly reverberates across those relationships that provide the ground of the individual's personhood. Brain research holds great promise in improving an individual's life, but could also present significant obstacles to human flourishing. For this reason, it is important for scientific teams to consider the following social and cultural aspects of their work and the data they generate.

1a. What are the possible unintended consequences of neuroscience research on social stigma and self-stigma?

It is necessary to consider how individualism and collectivism are articulated in a local context because these are predictors toward stigma and mental illness—for instance, collectivist beliefs have been positively correlated with stigma against mental illness (Papadopoulos et al., 2013). Researchers who deploy predictive models of disease and technological developments for preclinical detection of brain diseases should ask whether their work improves the quality of life in physical and social terms for those living with a disorder, or whether their predictions could unexpectedly exacerbate suffering. Addressing how such technologies might impact or alter individual self-understanding should be integral to research. For example, how does information about etiology or predictive assessments foster or undermine a person's sense of their agency? Does a prediction for a brain disease threaten to redefine a person's sense of their life trajectory? Could it change how they define their future selves? What new pressures or opportunities for treatment might such predictive information produce? Exploring how we conduct, apply, and communicate this research requires broader societal discussion. Collaborative research opportunities with neuroethicists could include developing methods for communicating with patients and their families about novel choices and decision points involving diagnoses or interventions. Researchers can look to the precedent established for embedding neuroethicists in experimental procedures like deep brain stimulation for depression. These embedded neuroethicists interview study participants about the participants' perceived benefit and comprehension of the complexities of the intervention (Leykin et al., 2011). Current NIH BRAIN projects include neuroethics grants exploring the ongoing ethical conundrums that arise when doing opportunistic brain recordings in patients who undergo surgical procedures for epilepsy (Chiong et al., 2018).

When exploring the question of unintended stigma, researchers should be able to articulate how their models of disease promote or adversely affect concepts of wellness or if these models create tensions or violate prevalent beliefs about wellness or disease. Within the Confucian cultural context, for example, family is the guiding metaphor for interpersonal relations—to address a collection of people in Chinese is to literally call for the attention of the "big family" (大家) (Chen and Fan, 2010). In many cultures guided by such a principle of interdependence, a condition like autism would stigmatize not only the individual but also an entire family; the social discrimination can jeopardize marriage and business prospects (Lauber and Rössler, 2007). While the impact of disease may be considered to universally draw concerns of loved ones and family members, in the Confucian context, such a disease or even a predictive assessment can impact families in a way that is much more foundationally shaking. Kleinman and Mechanic note that "mental illness in China is not a confidential relationship between patient and doctor, but a social issue involving the home, the work place and [broader community]" (Kleinman and Mechanic, 1981, p. 340). Further, they note that mental illness is considered first and foremost a public health problem and therefore warrants sharing the problems with family, neighbors, and co-workers (Kleinman and Mechanic, 1981, p. 348). As clinical research is ongoing, it is worth noting that, in the absence of access to interventions, a preclinical diagnosis of risk could be received as a sentence that condemns the entire family rather than an opportunity for an individual's therapeutic intervention. Exploring these questions can also be done through interdisciplinary collaborations using empirical methods to assess public views on these questions.

1b. Is it possible that social or cultural bias has been introduced in research design or in the interpretation of scientific results?

A stated aim of many of the brain projects is to better understand neural circuitry in the diseased and non-diseased human brain, with goals that include predicting, restoring, connecting, or enhancing brain function (Huang and Luo, 2015; Martin and Chun, 2016). Much neuroscientific research is focused on investigating what might be considered adverse or abnormal phenomena related to the brain, but notions of what is normal and abnormal, what is common or uncommon, and what is acceptable or unacceptable reflect social or cultural biases that are not universal and may require further justification. (Abi-Rached, 2008; Bird, 2012; Goering, 2018; Roy, 2012). For example, is the reductionism inherent (and often scientifically necessary) to the connectome and brain atlasing projects compatible with the variations found in lived human behavior and experience? Scientists can start these explorations at the very inception of their experimental design and note how assumptions might bias hypotheses. For example, some members of the neurodiversity movement (Jaarsma and Welin, 2012)—an advocacy position promoting autism as a natural variant of human neurological development—would consider research to cure autism a road to promoting eugenics. It is important to consider how socially constructed identities shape the experiments and questions chosen and the ways the data are interpreted. In that spirit, care must be taken to avoid studies that may reflect or replicate biases in society including negative biases toward race, ethnicity, gender, and disability. Because the findings of neuroscience are often interpreted as unique underpinnings of "human-ness," the stakes of misinterpreting the implications of neuroscience research are high. This is not to say that research

must be perspective-free or value-neutral. The act of addressing bias is one of addressing unacknowledged assumptions, implicit cultural norms, and underrepresented values in the research. When researchers reflexively reflect on their own particular views and include the voices of those with different perspectives, they work to achieve "strong objectivity"—objectivity that is achieved through a diverse range of perspectives (Harding, 2005). Neuroscience research can benefit from incorporating the input of a variety of stakeholders throughout the research process, particularly that of the potential consumers of new neurotechnologies. It is important to anticipate how findings could impact societal evaluations of diversity and inclusivity, and how scientific research has tried to account for biases, assumptions, and valuations in constructing the "normal" or "natural" brain since these qualities are frequently culturally determined. Taking into consideration existing social and cultural perspectives and differences concerning the continuum of wellness to illness can ensure sensitivity to diverse stakeholder public perspectives and that any resulting treatments are relevant and acceptable. For example, while memory decline may be considered to be a typical part of aging (Fjell et al., 2014), developments of technologies to improve memory in the diseased brain may lead to a market of interventions for enhancing what was once considered "normal" aging. The societal implications of pathologizing aging would be significant, considering that aging is universally part of the human experience.

Q2. What are the ethical standards of biological material and data collection; how do local standards compare to those of global collaborators?

In order to advance science and technology, a stated aim of most of the national-level brain initiatives is the creation of large data platforms to share knowledge and further collaborate (Devor et al., 2013). Such platforms require the collection and curation of large-scale data from both human and nonhuman sources on multiple levels. Indicative of this push is the proposal to create a massive data-sharing platform called the International Brain Station (http://www.kavlifoundation.org/kavli-news/kavli-foundation-commends-establishment-international-brain-initiative#.WpcHOIJG1Bw). The commitment of the national-level brain projects to the collaborative effort in the formation of the International Brain Initiative (IBI) has buoyed support for a project like the International Brain Station.

Data sharing raises a number of ethical and legal issues. Some of these issues have already been acknowledged and continue to be explored in other contexts (e.g., biobanking) and legislation on data protection and privacy exists in many countries and regions (e.g., General Data Protection Regulation 2016/679 EU). However, brain research and data sharing may raise issues not identified yet, and not covered by existing regulations. Some brain projects have begun to recommend protections and protocols given the sensitive nature of brain data. For example, the HBP has begun to address issues specific to data sharing within big science projects and has a number of resources on their site (https://www.humanbrainproject.eu/en/social-ethical-reflective/ethics-support/data-protection/). In the Data Protection and Privacy opinion from the HBP, in reference to the UNESCO report on respect for human vulnerability and integrity, they state that "respect for persons requires acknowledging people's autonomy, i.e., their capacity to make decisions and act on the basis of those decisions, and their integrity, i.e., the inviolability of their bodily and psychological self" (Rose et al., 2016, p. 7). Privacy and protections for biological material and data collection are consistently valued as a means to achieving autonomy or even as essential to human dignity. However, cultural perceptions of terms like autonomy and individual integrity, and the overall well-being of a society (Nissenbaum, 2009), can impact scientific practice and policies.

2a. How can human brain data (e.g., images, neural recordings, etc.), and the privacy of participants from whom data is acquired, be protected in case of immediate or legacy use beyond the experiment?

fMRI studies have demonstrated that it is possible to crudely reconstruct a set of images on which a participant has been trained (Nishimoto et al., 2011). More recently, a proof-of-principle study indicated the feasbility of conducting an Internet image search using a process of mentalizing the image (Naselaris et al., 2015). Researchers have also established methods to predict concepts and categories of words, and the word/number participants are imagining (Bauer and Just, 2017) with machine learning algorithms and fMRI. More recently, this same group has used this technique to identify suicidal ideation in youths (Just et al., 2017).

While there is general appreciation that participants in studies (and the public at large) have "privacy interests" that must be respected, the first ethical issue to address is *how* to conceptualize privacy with regard to brain-based data. Is the information acquired from the brain revealing or stigmatizing in ways that are unique compared to other bodily tissues or to psychological research? What are the principles underlying the obligation to respect privacy? These are questions that are motivated by the science and require engagment by scientists, and these questions can be investigated with an ethicist or scholar with appropriate interdisciplinary expertise to achieve some resolutions (Rose et al., 2016).

Further, whose privacy interest is at stake in the case of data sharing? Will sharing human brain data entail unjustifiably compromising the privacy interests of data donors? How can human brain data be shared without impacting such privacy interests? Like genetic data, some brain data, even when de-identified, holds the potential for identification of the study participant. Were this to happen, has a re-identified person's privacy been violated?

The public has expressed some privacy concerns around neurotechnology (Jebari and Hansson, 2013) and the acquisition of private information from neurotechnologies (Higashijima et al., 2011). In brain computer interface (BCI) research, privacy concerns have been discussed in the context of how to offer appropriate informed consent (Klein and Ojemann, 2016). In the case of increasingly large "big data" set analysis in neuroscience, it may be the case that maintaining de-identification (i.e., stripping information that will link data back to the individual) is no longer possible (Choudhury et al., 2014). The more likely possibility with large datasets or small numbers of initial participants is re-identification. In such cases, consent for participation in studies may need to acknowledge these realities. Further, as data are being shared into large-scale databases, and as we move toward

broad consent for data re-use, it is likely that data will be subject to additional uses beyond the initial study in which it was collected. In those cases, what are the moral considerations underlying the obligation to seek consent? Importantly, legacy use may impact not only the individual who provided the brain data, but also family members.

Even in the early stages of research, scientists can collaboratively ask—by engaging would-be consumers and neuroethicists—whether and how sharing human brain data can harm groups of people even if the privacy interests of data donors are not directly compromised. With regard to informed consent, is consent as traditionally conceived in bioethics (consent from the individual) applicable in this context? If not, how can one improve on the notion of consent so that it is useful? On the other hand, even when the risks to privacy violations may be high, one must also weigh those harms against what harm may come from withholding data; what harm may come from anonymizing or de-identifying data? Of course, often neuroscience researchers do not make decisions about privacy and risk in a vacuum. Human neuroscience studies funded by the BRAIN Initiative exist within a framework of federal oversight that includes robust human subject protections bound both by regulation and policy. However, these oversight frameworks do not divest researchers of the responsibility for considering these issues on their own. Insights and experience of researchers are critical to identifying hurdles in maintaining privacy or in determining what realistically can be kept de-identified in the near and long-term.

Exploring these issues can be particularly complex when navigating a variety of cultural and historical contexts because of the plurality of ways in which privacy may be defined, operationalized, and enforced (Miyashita, 2016; National Research Council, 2007). Variation in privacy policies not only reflects legal infrastructures, but also reinforces notions of self, trust, and liberty. As we consider notions of privacy and how they relate to data governance and reconciling differing governance and regulatory frameworks, it would be valuable to consider why such protections, if any, are in place, what are mechanisms of enforcement, and what precisely is meant by privacy rights. For example, in the EU we see more significant privacy considerations in law, but concerns for privacy revolved around preserving dignity of individuals (Whitman, 2004). In the US, both federal law (the Health Insurance Portability and Accountability Act, or HIPAA) and the 4th, 5th, and 14th Amendments to the Constitution guarantee and protect individual privacy in health-related contexts. Researchers collecting and using data must comply with HIPAA. However, many communities have a history of valuing public interests over individual ones. In Japan, privacy was historically viewed as selfish and to have privacy was to sacrifice community values; this is changing with a relatively recent shift in the 1960s to more focus on individual freedoms (Miyashita, 2011). As of 2002, a declaration of a "right to privacy" was introduced to Chinese Civil Code; however, the challenge in its implementation is that in the Chinese written language privacy (隐私) was historically translated as "shameful secrets" (Farrall, 2008). Such historical community values around notions of privacy and conceptualization of the role of the brain in personhood can illuminate the type and ways data are collected and stored, and how to begin conversations in navigating these shared and varied perspectives on permissibility of data collection and use.

2b. Should special regard be given to the brain tissue and its donors due to the origin of the tissue and its past?

Many of the national brain projects involve innovative ways of exploring the brain that will necessitate donations of human brains, brain tissue, brain data, or nonhuman animal brains. The creation of, acquisition of, and experimentation with these materials will bring the research community to new frontiers of permissibility and will likely present neuroscientists with the need to defend the appropriateness of the research being conducted.

The brain is a critical component in the development of human memory and experience, and thereby can be considered to carry the imprints of individual histories. It is unclear, however, whether, brain tissue (parts or the whole organ including organoids and brain material subject to radical tissue preservation procedures) should be viewed through the same moral lens as tissues collected from other organs. The greater the insights gained about the circuits and functioning systems of the brain, the more may be gleaned about the donors and their pasts. Even hippocampal preparations used to study memory formation may warrant special regard given that the electrical activity, the very contents (such as memories) in the tissue itself, might be considered by some to be intimately tied to the donor.

Many of the brain projects aspire to create and expand human brain banks and brain donation. While no brain bank in the world would likely consider itself to be in surplus, brain banks in many countries in East Asia are particularly sparse. Human brain tissue is seen by many scientists to be critical to better understanding the unique intricacies of the brain. To this end, brain banks provide a valued service to the neuroscience community. Donated human brains are a precious resource given both their scarcity and the logistical challenges for acquiring and preserving the tissue. Because of these scientific challenges, brains ideally would be collected locally (Graeber, 2008). Local collections highlight the need to address the cultural and religious values of the public who support this research, in order to negotiate and evaluate the growth and sustainability of brain banks, and perhaps whether brain banks might even be ethical (Yan et al., 2015). It is not an uncommon belief that the brain is in some manner connected to an individual's consciousness or even the self. In some cultures with a legacy of Buddhist traditions, there can be concern that removing a decedent's brain from the body could interfere with a peaceful transition after death (Yan et al., 2015). Furthermore, in societies with significant Confucian traditions it may be difficult to acquire any tissues from donors because of beliefs that a person's body does not ultimately belong to them, but rather to their parents. In this cultural orientation the potential organ donor has an obligation to their parents to maintain and preserve their bodily integrity (Fan, 1999). Collection and preparation of brain systems, either studies in whole brains or in proxies of parts and whole living brains, require ongoing bi-directional discussion with would-be donors, their families, ethicists, and scientists so that there can be shared awareness of prevailing values and beliefs around tissue donations as well as the realistic and evolving ethical uses of using these tissues experimentally.

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Q3. What is the moral significance of neural systems that are under development in neuroscience research laboratories?

Several of the brain projects emphasize development of neurotechnologies that serve as proxies of human brain circuits, such as human cerebral organoids, human/nonhuman chimeras, and BCIs. This could also be extended to nonhuman models such as purely computational models of the brain or nonhuman animal brains genetically engineered to be more "human-like." The human/nonhuman distinction becomes continually complicated with ongoing ethical and legal arguments pushing for rights of "personhood" (Andrews et al., 2018; Greene et al., 2005; Lavazza and Massimini, 2018) in nonhumans. As engineered neural circuits and systems become more complex, they may outstrip the ability of the research community to fully understand their new intrinsic abilities, leading perhaps to considerations of their moral status. What properties or functions would need to be present in order to prompt consideration about moral significance? There is a need to continually revisit whether and how new technologies enable the research community to assess these properties, i.e., unknown unknowns.

3a. What are the requisite or even minimum features of engineered neural circuitry required to generate a concern about moral significance?

Scientists may more deeply engage this question by considering how the tissue was acquired and how new models could and should be created. Given the critical role of the brain in human experience, should brain tissue (parts or the whole organ, and preparation of models such as induced pluripotent stem cell-derived cerebral organoids) be viewed as morally different from other organs? One simple exercise is for neuroscientists to ask themselves what the public response to the research may be. There is also a need to recognize that the socially accepted bounds today may change, or need to be revisited, as the science develops. Further, when considering engineered entities (e.g., manipulations to non-human animals, or even in some instances AI), what are the requisite or even minimum features that might trouble notions of personhood (Aach et al., 2017)?

The utility of using AI to interface with medical tools and devices is being increasingly demonstrated (Hainc et al., 2017); AI has been used with closed-loop BCIs to enhance memory (Ezzyat et al., 2018), and to faciliate movement (Orsborn et al., 2014), with the aims of making BCIs more accurate, adaptable, and convenient. One can anticipate a growing set of ethical issues as research on intelligent and socially assistive robots continues to advance, especially since these are a targets of several of the brain projects based in East Asia (Jeong et al., 2016; Okano et al., 2016; Poo et al., 2016). These robots have developed in divergent ways that reflect the values and concerns of their engineers, illustrating a divide in the field. There is a community of scientists who argue that robots must not look human-like until their intelligence can match that of humans (Darling, 2017). In parallel, leading researchers in Korea and Japan have created some of the most human-like socially interactive robots to date. Reports have suggested cultural differences: some Japanese publics have a stronger desire for humanoid robots over other forms of AI than some US publics (Sugiyama et al., 2017); Japan even houses the first all-robot run hotel (*Henn-na* Hotel, roughly translated as "weird" hotel) run by humanoid to dinosaur-form robots (Osawa et al., 2017). The global market for socially assistive robots for a world-wide growing aging population will bring further urgency to addressing these engineering and ethical divides over what we can create and how we should interact with these new technologies.

3b. Are the ethical standards for research conduct adequate and appropriate for the evolving methodologies and brain models?

There is value and there are translational limits when applying nonhuman animal research to humans (Hyman, 2012; Pankevich et al., 2014). Still, the (living/*in vivo*) brains of NHPs often represent the closest approximation of human brains (and behavior) available today. The advent of the genetically modified monkey model of autism and "autism-like behaviors" foregrounds the ethical question of whether the potential benefits justify creating human brain diseases and neurobehavioral states in nonhuman animal models (Liu et al., 2016; Neuhaus, 2018). If the nonhuman animal is "human enough" to model traits that seem so uniquely human, do they deserve the rights and protections afforded to humans in research? If the grounds for experimenting on these animals derive from the fact that they have a brain similar to ours, and the brain is the organ often considered to distinguish humans from other animals imbuing humans with their dignity, then to what degree ought we set limits on experimentation in these animals? Perhaps a greater concern is the possibility that researchers may be able to introduce capacities such as cognitive or emotional abilities that would further blur the line between the human and the nonhuman (Greely, 2011). A discussion of the blurring boundaries of personhood, especially with insights from engineering neural circuits, raises questions as to how new discoveries in neuroscience might alter our perceptions of the nonhumans that we use in research. To be clear, in general, the use of animals and data derived from nonhuman animal studies receives regulatory attention and there are already numerous mechanisms in place for oversight of nonhuman animal research. However, with brain research, engineering, and modification, there may be a need to take into account special ethical considerations as new considerations for animal welfare may arise. Might we need a separate category of regulation for nonhuman animals engineered to have more human-like characteristics? Do we need to rethink the human/nonhuman distinction in research ethics as neuroscience methodologies evolve?

Given the explicit interest among these national brain projects for data sharing, how can researchers reconcile the differences in regulatory and welfare standards and perspectives about what traits might afford changes in "moral status" in the organism of study among a plurality of national values and standards? As stated above, NHP research is now a focus of some projects in East Asia (Okano et al., 2016; Poo et al., 2016) while this research is increasingly controversial among US (Funk and Rainie, 2015) and European (European Commission, 2010) publics. The sharing of brain data between countries that hold different ethical stances on what is considered appropriate animal experimentation raises additional questions. Should a country accept or use data collected elsewhere in a fashion that is not considered locally ethical? How would this be operationalized in

large global brain initiatives such as the HBP or other large data-sharing platforms for neuroscience?

Regulation often reflects the complexity of religious, social, and politicial realities. In the proceedings of an international meeting held by the National Research Council about animal research in a global environment, one of the Chinese speakers advocated for a personal connection (for non-Chinese collaborators) to understand the people behind the research: ''I would like to offer a few additional suggestions for those planning to work with Chinese entities. The first is that it is important to spend more time going to China, and not just for site visits. It is important to spend time with the people who work there'' (ILAR, 2008).

Even when researchers have the training, expertise, resources, and desire to accommodate foreign standards for nonhuman animal research, their research is conducted within a complicated political backdrop of competing public values (ILAR, 2008) that intersect with broader questions about equity and resource allocation. Quoting from a *Cell* commentary, ''There are 135 million Chinese living on less than $1 a day, which the World Bank defines as abject poverty. In comparison, 'monkeys listen to music, have toys to play with and drink purified water'' (Hao, 2007, p. 1035). This is not to suggest that the standards of NHP work are inappropriate, but to state that broader issues about equity and resource allocation can also impact local public support of science. Deeper exploration of the values underlying the regulations and discussions about overarching issues of equity and resource allocation can lead to more fruitful dialogs on shared views, goals, and best practices for scientific collaborations.

Q4. How could brain interventions impact or reduce autonomy?

Many of the national brain projects aim to better understand and intervene on brain function. This section is concerned with the use of neural interventions that have the capacity to modify a participant's personality, affective states, cognition, behavior, autonomy, agency, and other significant effects (Ineichen and Christen, 2015). Some interventions are explicitly designed to change affective states such as deep brain stimulation for depression. How and to what extent the brain is considered related to or responsible for these features of human experience is an important cross-cultural consideration.

4a. What measures can be in place to ensure optimal autonomy and agency for participants/users?

The answer requires conceptually unpacking the notions of ''agency'' and ''autonomy.'' What comprises an ''agent'' who is able to freely, of their own volition, choose to act in this world? A large body of neuroscience research has focused on mechanisms of volition (Montague, 2007), decision-making, and study of how conscious intention and will, or lack thereof, can translate into action (Lavazza, 2016). As new devices and brain interventions are engineered, how can they empower users particularly given that some of these devices might be able to bypass conscious participation such as with an implanted brain stimulation device? A precedent for greater user control can be found with deep brain stimulation, which allows users to turn stimulation off during sleep in order to preserve battery life. On the other hand, some have argued that giving users control of their devices could potentially lead to harm to themselves and others should the device malfunction (Brown et al., 2016). Data collected from public participants as well as individuals who have brain computer interfaces reveal complicated interpretations of how the brain might be involved with their free will in degree and kind (Nahmias et al., 2014), and how brain devices might interfere with their sense of being the authors of their own actions (Klein et al., 2016). How to conceive agency, autonomy, self, and even responsibility as they relate to the brain is far from universally agreed upon within and across the communities in which these brain research projects are occurring (Descartes, 1985; Gillihan and Farah, 2005; Kitayama and Park, 2010; Nisbett and Miyamoto, 2005; Sakura, 2012; Vidal, 2009; Yang and Miller, 2015; Yu, 2009). In some cultures, autonomy may be considered a collective, rather than an individual capacity. Examples of collective autonomy in healthcare decision-making are evident in the common practice in some cultures of delivering diagnoses of terminal diseases to the head of the family rather than the patient, wherein the family—rather than the patient—will make decisions about interventions for the patient (Tai and Lin, 2001). Designing these interventions will require careful consideration of the most appropriate balance of user control, involving discussion as a team of scientists, ethicists, patients, and families. How can the user be empowered while keeping them physically and psychologically safe? This evaluation will also necessarily involve conceptual views of weighing the role of the brain in free will, personhood, and responsibility (see discussion in Culturally Informed and Aware Neuroethics: An Integrated Approach?).

4b. Who will have responsibility for effects (where responsibility has broad meaning encompassing legal, economic, and social contexts) of brain interventions?

To a large extent, legal responsibility depends on local legal, regulatory, and policy frameworks. However, laws and regulation are meant to reflect public values and, over time, can cease to keep pace with evolving public perspectives and moral beliefs. As such, moral responsibility is much more complex and involves cultural and societal notions about approriate action, intentions, and character. Underlying all views of responsibility is the assumption that those responsible have some sense and ability to exert control, which, as indicated above, neural devices potentially undermine. An added complexity is how one might experience the integration of one's self with a neural device when one's decision making and actions involve a neural device, and the boundaries of where the device and person begin and end are blurry. Further, in some cultures, ascribing responsibility to the participant as an individual may be less important than identifying the relational, environmental, and social conditions that led to an inappropriate behavior.

Mention of neuroscience in US courts has doubled from 2005 to 2012 (Farahany, 2016), reflecting public perceptions of the utility of using the brain as a way to assess agency, autonomy, and ultimate reponsibility. By contrast, in a preliminary study of a 1,000-person sample of the Taiwanese public, Wu found that knowledge of a brain disease or abnormality would not change the responsibility attribution for criminal acts, particularly for those individuals who professed Confucian beliefs (Wu, 2015). It remains to be seen how brain interventions might or might not shift the public's view of responsibility.

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Q5. In which contexts might a neuroscientific technology/innovation be used or deployed?

As is often the case with new technologies, many of those under the auspices of these national brain initiatives will have applications beyond the research agenda that was initially pursued. In neuroscience, technologies developed for medical use have potential uses in national defense, and the transfer of medical technologies to the commercial or legal domains are realities to be expected. While some of the brain projects, like the US BRAIN Initiative, have partners with entities dedicated to national security, such collaboration is *prima facie* avoided by the HBP. The European Commission classifies dual-use goods, products, and technologies as those "normally used for civilian purposes, but which may have military applications" (European Commission, 2010), and the rules for the EU's Horizon 2020 (under which the HBP is sponsored) state that research must have solely civilian applications (http://ec.europa.eu/research/participants/data/ref/h2020/other/hi/guide_research-civil-apps_en.pdf). However, this in itself does not rule out collaboration with defense-related organizations insofar as the goal is to focus on civilian applications. In addition, the open data policy of the HBP, and its commitment to creating large integrated platforms of information for broader use, in practical terms may limit a project's ability to prevent undesirable uses of its research. Thus, the Ethics and Society subproject undertook research to analyze not only the ethical and philosophical implications of the relevant research, but also the strengths, weaknesses, and ambiguities of existing definitions of dual use to produce a forthcoming recommendation to the HBP.

Driven by both private industry and the do-it-yourself community, there has also been a proliferation of wellness and enhancement applications (Fitz and Reiner, 2015) of tools that originated in the neuroscience research and medical space. There are genuine strengths in public-private partnerships given the financial resources and speed at which research and translation can occur. The complicated reality is that neuroscience innovations will not be used solely for clinical purposes, which makes the risk-to-benefit calculation less obvious.The sale and promotion of neurotechnological devices to enhance cognition and behavior often fall between the cracks of many existing medical regulatory systems, as the devices are not claimed to treat a medical condition. The requirement to demonstrate the effectiveness of commercial devices is largely absent in most regulatory frameworks (Riggall et al., 2015; Wexler, 2015). With the global brain projects alone, the scientific research community spans four continents; therefore, it is necessary to ask how both our local and broader communities respond to these potential multiple uses of these technologies. Scientists, as stewards of their work, should therefore consider and anticipate the potential impact of using technologies in non-clinical contexts, and engage with the public on these issues. This, of course, is an exercise that can and should involve partnership with an interdisciplinary team including sociologists and ethicists.

5a. Which applications might be considered misuse or best uses beyond the laboratory?

Part of scientific stewardship should include maintaining vigilance about the applications on the horizon and scientists are often best positioned to anticipate applications of their work. This mandate is not meant to forestall innovation or constrain academic freedom for scientists, but rather a call to be mindful of the shifting landscape of the scientific enterprise insofar as it is shaped by human and social values. One initial way to approach this task is for scientists to ask themselves why the public might consider them responsible for potential misuses of these technologies. What potential uses of the technology could raise societal concerns and why? Could the research enable technology that could be deployed in a problematic way? In particular, in a competitive funding environment it is important to give careful thought to the funder's role in determining intentional or unexpected misuse from the beginning. Consider calls for research exploring memory or cognitive enhancement. Memory enhancement in a military setting might be desirable for minimizing injuries in war. However, memory enhancement technologies in a commercial setting might create undue implicit coercion of individuals in the civilian environment to aspire to a "new normal" of enhanced ability (Hyman, 2011). While "academic enhancement" is the goal of many interventions, such as private schooling and academic coaching that give individuals with the necessary resources an advantage, the question is whether direct neural interventions are unique or exceptional in their abilty to enhance cognition or performance, and in their risks to users. There is a dearth of information on the long-term effects of non-medical use of these brain interventions.

The locations and sites for development of technologies will be influenced by the local values of the people and publics supporting that work. For instance, some stated reservations about enhancement often revolve around maintaining authenticity, i.e., reflecting a priority to preserve one's individual identity (Schelle et al., 2014). Preliminary studies in China, however, suggest that student's top concerns regarding cognitive enhancement tend to revolve around fairness with the lowest ranking concern being around preserving identity or violations of autonomy (Lan, 2015). These studies reflect what concerns are weighed in the risk-benefit analysis of such technologies and how they may vary across cultures. There is also a repeated trend in European regulations in health and science of adopting a precautionary, better safe than sorry approach (European Commission, 2017). Conventional belief in some regulatory circles is that the EU can be characterized as taking a more precautionary approach whereas the US takes a more proactive approach (ie., innovate in the absence of provable harm) with regard to risk evaluation (Wiener and Roger, 2002). Regardless, once the research is completed and published, it may matter less where the science originally was conducted as the data and their attendant products could be used by anyone who has access to the publications. As such, an anticipatory approach, including ongoing dialog between multiple stakeholders, is needed as part and parcel of neuroscience innovation.

5b. Does this research raise different and unique equity concerns and, if so, have equitable access and benefit of stakeholders been considered?

Under this question, scientists can start by asking whether their work, compared to other kinds of biomedical science, is able to modify foundational human capacities, and therefore raises unique ethical concerns. We have already seen a proliferation of "neuro-enhancement" technologies originally designed and

researched for therapeutic reasons that have been adopted by consumer industries such as tDCS (Wexler, 2015) and off-label use of "smart drugs" by students, academics, and others (Farah et al., 2004). Concerns about the use of cognitive enhancement circle around medical safety, coercion, and fairness (Schelle et al., 2014). Studies exploring public opinions on the use, applications, and ethical stances on the use of brain interventions have largely been limited to Western cultures while there is a notable paucity of studies representing East Asian populations. This lack of research may in part be due to lower popularity and knowledge of cognitive enhancement in East Asia compared to Europe and the US. That said, the South Korean Ministry of Food and Drug safety issued a warning in fall 2017 about the misuse of ADHD-related drugs for the purposes of cognitive enhancement, and one study demonstrated a seasonal trend in South Korea in prescribing ADHD medications that may co-occur during exam periods (Song and Shin, 2016).

Generally in studies of cognitive enhancement practices, physical safety and harm are leading concerns; further concerns include how coercion could impact the freedom to decide about one's life (Schelle et al., 2014). A preliminary study of a Taiwanese public population exploring the impact of Confucian belief systems on opinions about enhancement indicates that the gravest ethical concerns revolve around notions of violation of nature and disrespecting the gifts passed down through ancestors at birth (Wu, 2016). These data point to how ethical acceptability and attendant concerns of enhancement technologies could impact their development and ultimate clinical and consumer bases. Engaging the public will be critical in deliberating on what constitutes public benefit and public harm as neuroscience innovation leaves the walls of the laboratory and the clinic. Part of this work can be carried out with formal empirical research, and part of this work can be achieved through outreach and public forums. Stakeholder engagement can occur alongside technology development as has been demonstrated with the HBP through their collaborations with the Danish Board of Technology (http://hbp.tekno.dk/). Public understanding of and engagement with science, as has been substantively shown, vary enormously across and within countries, and are strongly influenced by access to resources and education (Bauer et al., 2012).

Conclusion and A Way Forward

The five central issues and related questions we identified with the presented NeQNs suggest that developing a more global and culturally aware neuroethics framework will need to include three aspects.

Greater Inclusivity

The goal of the Global Neuroethics Summit (GNS) is to begin an inclusive conversation regarding cultures and stakeholders in neuroethics. Initial GNS conversations are focused on the existing or in-development large-scale neuroscience research projects. As we move forward we expect that a more directed effort within the national brain projects will make the task of resourcing and implementing initially more manageable and help establish a stronger foundation for cross-cultural neuroethics. Long-term goals include a conversation beyond the scope of the brain projects, and in so doing, greater representation of a more diverse range of perspectives and stakeholders. To that end, we anticipate future meetings that include representatives from developing countries where some of this research is or could be conducted, as well as engaging partners beyond the government sector. These conversations will necessarily involve cultural scholars who can communicate unique and shared cultural perspectives on brain health, the brain, and its relationship to constructions of mind in particular. Engaging broader issues of equity, resource allocation, and distributive justice will be critical to future conversations as well.

Education

Neuroethics is a rapidly growing new field, just over a decade old, and there are still few formal neuroethics teaching resources. While both students and faculty engaged in neuroscience research have reported a desire for neuroethics training (Kehagia et al., 2012; Lombera et al., 2010; Sahakian and Morein-Zamir, 2009), US federal mandates for Responsible Conduct of Research ethics training for scientists and engineers, for example, are still relatively new and emphasize research ethics, rather than neuroethics (HHS, 1999; National Science Foundation, 2009). Many current faculty members have received little to no formalized training in ethics, much less training in neuroethics. The Australia Brain Alliance, the EU's Human Brain Project, and the US BRAIN Initiative have established neuroethics components that work to raise awareness and advance research of neuroethical issues with the researchers funded by their respective governments. The Korea Brain Initiative plans to formally integrate neuroethics education into neuroscientist training. Future work within the national brain projects will determine what formal neuroethics training resources will need to be developed. Importantly, neuroethics education should include raising awareness of shared and differing values across cultures and allow for critical engagement. Engagement with diverse stakeholders, particularly with representatives from developing countries, will be critical to achieving this goal.

Policy and Public Communication

Building a culturally aware neuroethics and neuroscience community will need to include engagement with understanding cultural and moral values and how to manage the tensions that will arise across transnational regulatory networks, especially when competing values and commitments are present. In one ideal form, policy reflects the will of the people, but not all nations share this ideal or implement it to the same degree. Moreover, even in countries that are governed by a system that prioritizes democratic ideals, the will and preference of the public will be determined in part by what they understand about science. That said, the public is not an empty vessel, nor are they entirely uninformed about science, and such a "deficit model" of communication has been recognized as unfruitful when engaging the public (Brown, 2009). Instead, a commitment to designing robust dialog and exchange between scientists and the publics they engage is needed. It is important to recognize that communication of science is an enormous challenge and its own rich area of research (Berg and Lidskog, 2018; Dietz, 2013; Illes et al., 2010). We aim to deepen these ongoing discussions and merge these efforts with scholarly and empirical studies to assess stakeholder views with a cultural analysis of existing guidelines.

As the horizon of what is known about the human brain and behavior expands, so grows the worldwide impact of

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neuroscience findings on health and healthcare, legal systems, national security, and consumer domains. Neuroethical concerns are fundamentally concerns about how neuroscience is designed and conducted and how neuroscience findings can be interpreted and translated into the lives of individuals acting in societies. Neuroethics is not only a reaction to rapidly evolving discoveries; it is also a driver of ethical innovation interwoven throughout neuroscience research and its translations. As such, neuroethics can be an essential tool for responsible research and enhancing neuroscience by serving in a horizon-scanning function, anticipating and addressing the ethical roadblocks ahead and facilitating discussions about ethical goals for neuroscience. Ultimately, this can help advance and accelerate an ethically tenable globalized neuroscience.

Our group is now working collaboratively with and supporting the development of the International Brain Initiative (Kavli Foundation, 2017). Building a culturally aware neuroethics community that prioritizes equitable representation of national interests and perspectives can have immediate real-world impact on neuroscience research and policy at the global level. Implementation of these questions within the individual brain projects will be the subject of our next Global Neuroethics Summit in fall 2018.

SUPPLEMENTAL INFORMATION

Supplemental Information includes one table and delegate affiliations and can be found with this article online at https://doi.org/10.1016/j.neuron.2018.09.021.

CONSORTIA

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REFERENCES

Aach, J., Lunshof, J., Iyer, E., and Church, G.M. (2017). Correction: Addressing the ethical issues raised by synthetic human entities with embryo-like features. eLife *6*, 6.

Abi-Rached, J.M. (2008). The implications of the new brain sciences. The 'Decade of the Brain' is over but its effects are now becoming visible as neuropolitics and neuroethics, and in the emergence of neuroeconomies. EMBO Rep. *9*, 1158–1162.

Amunts, K., Ebell, C., Muller, J., Telefont, M., Knoll, A., and Lippert, T. (2016). The Human Brain Project: creating a European research infrastructure to decode the human brain. Neuron *92*, 574–581.

Andrews, K., Comstock, G.L., Crozier, G.K.D., Donaldson, S., Fenton, A., John, T.M., Johnson, L.S.M., Jones, R.C., Kymlicka, W., Meynell, L., et al. (2018). Chimpanzee Rights: The Philosophers' Brief (Routledge).

Arias, J.J., Sarrett, J.C., Gonzalez, R., and Walker, E.F. (2018). The ethics of prodromal and preclinical disease stages. In The Routledge Handbook of Neuroethics, L. Johnson and K.S. Rommelfanger, eds. (Routledge).

Asai, A., Kadooka, Y., and Aizawa, K. (2012). Arguments against promoting organ transplants from brain-dead donors, and views of contemporary Japanese on life and death. Bioethics *26*, 215–223.

Aspinwall, L.G., Brown, T.R., and Tabery, J. (2012). The double-edged sword: does biomechanism increase or decrease judges' sentencing of psychopaths? Science *337*, 846–849.

Bauer, A.J., and Just, M.A. (2017). A brain-based account of "basic-level" concepts. Neuroimage *161*, 196–205.

Bauer, M.W., Shukla, R., and Allum, N. (2012). The Culture of Science: How the Public Relates to Science across the Globe, First Edition (London, UK: Routledge).

Berg, M., and Lidskog, R. (2018). Deliberative democracy meets democratised science: a deliberative systems approach to global environmental governance. Env. Polit. *27*, 1–20.

Bird, S.J. (2012). Potential for bias in the context of neuroethics. Commentary on "Neuroscience, neuropolitics and neuroethics: the complex case of crime, deception and fMRI". Sci. Eng. Ethics *18*, 593–600.

Brosnan, C. (2011). The sociology of neuroethics: expectational discourses and the rise of a new discipline. Sociol. Compass *5*, 287–297.

Brown, S. (2009). The new deficit model. Nat. Nanotechnol. *4*, 609–611.

Brown, T., Moore, P., Herron, J., Thompson, M., Bonaci, T., Chizeck, H., and Goering, S. (2016). Personal responsibility in the age of user-controlled neuroprosthetics. 2016 IEEE International Symposium on Ethics in Engineering. Science and Technology.

Burton, O.R. (2007). Why bioethics cannot figure out what to do with race. Am. J. Bioeth. *7*, 6–12.

Chattopadhyay, S., and De Vries, R. (2008). Bioethical concerns are global, bioethics is Western. Eubios J. Asian Int. Bioeth. *18*, 106–109.

Chattopadhyay, S., and De Vries, R. (2013). Respect for cultural diversity in bioethics is an ethical imperative. Med. Health Care Philos. *16*, 639–645.

Check, E. (2007). Cloning special: Dolly: a hard act to follow. Nature *445*, 802.

Chen, X., and Fan, R. (2010). The family and harmonious medical decision making: cherishing an appropriate Confucian moral balance. J. Med. Philos. *35*, 573–586.

Chen, S.X., and Mak, W.W. (2008). Seeking professional help: etiology beliefs about mental illness across cultures. J. Couns. Psychol. *55*, 442–450.

Chiong, W., Leonard, M.K., and Chang, E.F. (2018). Neurosurgical patients as human research subjects: ethical considerations in intracranial electrophysiology research. Neurosurgery *83*, 29–37.

Choudhury, S., Nagel, S.K., and Slaby, J. (2009). Critical neuroscience: linking neuroscience and society through critical practice. Biosocieties *4*, 61–77.

Choudhury, S., Fishman, J.R., McGowan, M.L., and Juengst, E.T. (2014). Big data, open science and the brain: lessons learned from genomics. Front. Hum. Neurosci. *8*, 239.

Darling, K. (2017). "Who's Johnny?" Anthropomorphic framing in human–robot interaction, integration, and policy. In Robot Ethics 20 (Oxford University Press).

De Vries, R. (2005). Framing neuroethics: a sociological assessment of the neuroethical imagination. Am. J. Bioeth. *5*, 25–27, discussion W3-4.

Descartes, R. (1985). The Philosophical Writings of Descartes (Cambridge University Press).

Devor, A., Bandettini, P.A., Boas, D.A., Bower, J.M., Buxton, R.B., Cohen, L.B., Dale, A.M., Einevoll, G.T., Fox, P.T., Franceschini, M.A., et al. (2013). The challenge of connecting the dots in the B.R.A.I.N. Neuron *80*, 270–274.

Dietz, T. (2013). Bringing values and deliberation to science communication. Proc. Natl. Acad. Sci. USA *110* (*Suppl 3*), 14081–14087.

Eric, R., and Matthew, S. (2017). The competing identities of neuroethics. The Routledge Handbook of Neuroethics (Routledge).

European Commission (2010). Eurobarometer: science and technology report, pp. 60-64, http://ec.europa.eu/commfrontoffice/publicopinion/archives/ebs/ebs_340_en.pdf.

European Commission (2017). Future brief: the precautionary principle: decision-making under uncertainty. In Science for Environment Policy (European Commission's Directorate - General Environment).

Evers, K. (2016). The contribution of neuroethics to international brain initiatives. Nat. Rev. Neurosci. *18*, 1–2.

Evers, K., Salles, A., and Farisco, M. (2017). Theoretical framing of neuroethics: the need for a conceptual approach. In Debates About Neuroethics (Springer), pp. 89–107.

Ezzyat, Y., Wanda, P.A., Levy, D.F., Kadel, A., Aka, A., Pedisich, I., Sperling, M.R., Sharan, A.D., Lega, B.C., Burks, A., et al. (2018). Closed-loop stimulation of temporal cortex rescues functional networks and improves memory. Nat. Commun. *9*, 365.

Fan, R. (1999). Confucian Bioethics (Kluwer Academic Publishers).

Farah, M.J., Illes, J., Cook-Deegan, R., Gardner, H., Kandel, E., King, P., Parens, E., Sahakian, B., and Wolpe, P.R. (2004). Neurocognitive enhancement: what can we do and what should we do? Nat. Rev. Neurosci. *5*, 421–425.

Farahany, N.A. (2016). Neuroscience and behavioral genetics in US criminal law: an empirical analysis. J. Law Biosci. *2*, 485–509.

Farrall, K.N. (2008). Global privacy in flux: illuminating privacy across cultures in China and the U.S. Int. J. Commun. *2*, 993–1030.

Fitz, N.S., and Reiner, P.B. (2015). The challenge of crafting policy for do-it-yourself brain stimulation. J. Med. Ethics *41*, 410–412.

Fjell, A.M., McEvoy, L., Holland, D., Dale, A.M., and Walhovd, K.B.; Alzheimer's Disease Neuroimaging Initiative (2014). What is normal in normal aging? Effects of aging, amyloid and Alzheimer's disease on the cerebral cortex and the hippocampus. Prog. Neurobiol. *117*, 20–40.

Funk, C., and Rainie, L. (2015). Public and scientists' views on science and society, http://www.pewinternet.org/2015/01/29/public-and-scientists-views-on-science-and-society/.

Garden, H., and Winickoff, D. (2018). Issues in neurotechnology governance. https://doi.org/10.1787/c3256cc6-en.

Gillihan, S.J., and Farah, M.J. (2005). Is self special? A critical review of evidence from experimental psychology and cognitive neuroscience. Psychol. Bull. *131*, 76–97.

Goering, S. (2018). Thinking differently: neurodiversity and neural engineering. In Handbook of Neuroethics, L. Johnson and K.S. Rommelfanger, eds. (Routledge), pp. 37–50.

Goldschmidt, R., and Renn, O. (2006). Meeting of Minds – European Citizens' Deliberation on Brain Sciences: Final Report of the External Evaluation (Universitat Stuttgart).

Graeber, M.B. (2008). Twenty-first century brain banking: at the crossroads. Acta Neuropathol. *115*, 493–496.

Greely, H.T. (2011). Human/Nonhuman Chimeras: Assessing the Issues (Oxford University Press).

Greene, M., Schill, K., Takahashi, S., Bateman-House, A., Beauchamp, T., Bok, H., Cheney, D., Coyle, J., Deacon, T., Dennett, D., et al. (2005). Ethics: moral issues of human-non-human primate neural grafting. Science *309*, 385–386.

Grillner, S., Ip, N., Koch, C., Koroshetz, W., Okano, H., Polachek, M., Poo, M.M., and Sejnowski, T.J. (2016). Worldwide initiatives to advance brain research. Nat. Neurosci. *19*, 1118–1122.

Hainc, N., Federau, C., Stieltjes, B., Blatow, M., Bink, A., and Stippich, C. (2017). The bright, artificial intelligence-augmented future of neuroimaging reading. Front. Neurol. *8*, 489.

Hao, X. (2007). Monkey research in China: developing a natural resource. Cell *129*, 1033–1036.

Harding, S. (2005). Rethinking standpoint epistemology: what is "strong objectivity?". In Feminist Theory: A Philosophical Anthology, A.E. Cudd and R.O. Andreasen, eds. (Oxford: Blackwell Publishing), pp. 218–236.

Heffernan, O. (2010). 'Climategate' scientist speaks out. Nature *463*, 860.

HHS (1999). Public Health Service, Policy on Instruction in Responsible Conduct in Research (U.S. Department of Health and Human Services).

Higashijima, J., Takahashi, K., and Kato, K. (2011). Ethical and social concerns: opinions of Japanese life-science researchers on developments in the science of mind and behavior. East Asian science, technology and society. Int. J. *5*, 359–374.

Huang, Z.J., and Luo, L. (2015). Neuroscience. It takes the world to understand the brain. Science *350*, 42–44.

Hyman, S.E. (2011). Cognitive enhancement: promises and perils. Neuron *69*, 595–598.

Hyman, S.E. (2012). Revolution stalled. Sci. Transl. Med. *4*, 155cm11.

ILAR (2008). Animal research in a global environment: meeting the challenges. Proceedings of the November 2008 International Workshop (National Research Council Institute for Laboratory Animal Research).

Illes, J., Moser, M.A., McCormick, J.B., Racine, E., Blakeslee, S., Caplan, A., Hayden, E.C., Ingram, J., Lohwater, T., McKnight, P., et al. (2010). Neurotalk: improving the communication of neuroscience research. Nat. Rev. Neurosci. *11*, 61–69.

Ineichen, C., and Christen, M. (2015). Analyzing 7000 texts on deep brain stimulation: what do they tell us? Front. Integr. Nuerosci. *9*, 52.

Jaarsma, P., and Welin, S. (2012). Autism as a natural human variation: reflections on the claims of the neurodiversity movement. Health Care Anal. *20*, 20–30.

Jebari, K., and Hansson, S.O. (2013). European public deliberation on brain machine interface technology: five convergence seminars. Sci. Eng. Ethics *19*, 1071–1086.

Jeong, S.J., Lee, H., Hur, E.M., Choe, Y., Koo, J.W., Rah, J.C., Lee, K.J., Lim, H.H., Sun, W., Moon, C., and Kim, K. (2016). Korea Brain Initiative: integration and control of brain functions. Neuron *92*, 607–611.

Jorgenson, L.A., Newsome, W.T., Anderson, D.J., Bargmann, C.I., Brown, E.N., Deisseroth, K., Donoghue, J.P., Hudson, K.L., Ling, G.S., MacLeish, P.R., et al. (2015). The BRAIN Initiative: developing technology to catalyse neuroscience discovery. Philos. Trans. R. Soc. Lond. B Biol. Sci. *370*, https://doi.org/10.1098/rstb.2014.0164.

Just, M.A., Pan, L., Cherkassky, V.L., McMakin, D., Cha, C., Nock, M.K., and Brent, D. (2017). Machine learning of neural representations of suicide and emotion concepts identifies suicidal youth. Nat. Hum. Behav. *1*, 911–919.

Kavli Foundation (2017). International Brain Initiative, http://www.kavlifoundation.org/international-brain-initiative.

Kehagia, A.A., Tairyan, K., Federico, C., Glover, G.H., and Illes, J. (2012). More education, less administration: reflections of neuroimagers' attitudes to ethics through the qualitative looking glass. Sci. Eng. Ethics *18*, 775–788.

Kitayama, S., and Park, J. (2010). Cultural neuroscience of the self: understanding the social grounding of the brain. Soc. Cogn. Affect. Neurosci. *5*, 111–129.

Klein, E., and Ojemann, J. (2016). Informed consent in implantable BCI research: identification of research risks and recommendations for development of best practices. J. Neural Eng. *13*, 043001.

Klein, E., Goering, S., Gagne, J., Shea, C.V., Franklin, R., Zorowitz, S., Dougherty, D.D., and Widge, A.S. (2016). Brain-computer interface-based control of closed-loop brain stimulation: attitudes and ethical considerations. Brain-Computer Interfaces *3*, 140–148.

Kleinman, A., and Mechanic, D. (1981). Mental illness and psychosocial aspects of medical problems in China. In Normal and Abnormal Behavior in Chinese Culture, A. Kleinman and T.-Y. Lin, eds. (Springer Netherlands), pp. 331–356.

Kvaale, E.P., Haslam, N., and Gottdiener, W.H. (2013). The 'side effects' of medicalization: a meta-analytic review of how biogenetic explanations affect stigma. Clin. Psychol. Rev. *33*, 782–794.

Lan, M. (2015). Analysis of Chinese College students' attitudes towards cognitive enhancement in education. International Conference on Social Science. Education Management and Sports Education.

Lauber, C., and Rössler, W. (2007). Stigma towards people with mental illness in developing countries in Asia. Int. Rev. Psychiatry *19*, 157–178.

Lavazza, A. (2016). Free will and neuroscience: from explaining freedom away to new ways of operationalizing and measuring it. Front. Hum. Neurosci. *10*, 262.

Lavazza, A., and Massimini, M. (2018). Cerebral organoids: ethical issues and consciousness assessment. J. Med. Ethics *44*, 606–610.

Leykin, Y., Christopher, P.P., Holtzheimer, P.E., Appelbaum, P.S., Mayberg, H.S., Lisanby, S.H., and Dunn, L.B. (2011). Participants' perceptions of deep brain stimulation research for treatment-resistant depression: risks, benefits, and therapeutic misconception. AJOB Prim. Res. *2*, 33–41.

Liang, P., Xu, Y., Zhang, X., Ding, C., Huang, R., Zhang, Z., Lv, J., Xie, X., Chen, Y., Li, Y., et al. (2015). CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes. Protein Cell *6*, 363–372.

Liu, Z., Li, X., Zhang, J.T., Cai, Y.J., Cheng, T.L., Cheng, C., Wang, Y., Zhang, C.C., Nie, Y.H., Chen, Z.F., et al. (2016). Autism-like behaviours and germline transmission in transgenic monkeys overexpressing MeCP2. Nature *530*, 98–102.

Lombera, S., Fine, A., Grunau, R.E., and Illes, J. (2010). Ethics in neuroscience graduate training programs: views and models from Canada. Mind Brain Educ. *4*, 20–27.

Martin, C.L., and Chun, M. (2016). The BRAIN Initiative: building, strengthening, and sustaining. Neuron *92*, 570–573.

Miyashita, H. (2011). The evolving concept of data privacy in Japanese law. International Data Privacy Law *1*, 229–238.

Miyashita, H. (2016). A tale of two privacies: enforcing privacy with hard power and soft power in Japan. In Enforcing Privacy Law, Governance and Technology Series, D. Wright and P. De Hert, eds. (Springer), pp. 105–122.

Montague, P.R. (2007). Neuroeconomics: a view from neuroscience. Funct. Neurol. *22*, 219–234.

Nahmias, E., Shepard, J., and Reuter, S. (2014). It's OK if 'my brain made me do it': people's intuitions about free will and neuroscientific prediction. Cognition *133*, 502–516.

Naselaris, T., Olman, C.A., Stansbury, D.E., Ugurbil, K., and Gallant, J.L. (2015). A voxel-wise encoding model for early visual areas decodes mental images of remembered scenes. Neuroimage *105*, 215–228.

National Research Council (2007). In Engaging Privacy and Information Technology in a Digital Age, J. Waldo, H.S. Lin, and L.I. Millett, eds. (The National Academies Press), p. 450.

National Science Foundation (2009). America Creating Opportunities to Meaningfully Promote Excellence in Technology, Education, and Science (COMPETES) Act; Section 7009 Responsible Conduct of Research (National Science Foundation).

Neuhaus, C.P. (2018). Ethical issues when modelling brain disorders in non-human primates. J. Med. Ethics *44*, 323–327.

Nisbett, R.E., and Miyamoto, Y. (2005). The influence of culture: holistic versus analytic perception. Trends Cogn. Sci. *9*, 467–473.

Nishimoto, S., Vu, A.T., Naselaris, T., Benjamini, Y., Yu, B., and Gallant, J.L. (2011). Reconstructing visual experiences from brain activity evoked by natural movies. Curr. Biol. *21*, 1641–1646.

Nissenbaum, H. (2009). Privacy in Context: Technology, Policy, and the Integrity of Social Life (Stanford University Press).

Normile, D. (2018). China's ambitious brain science project inches forward. Science *360*, 840–841.

OECD (2017). Neurotechnology and society. In OECD: Science, Technology and Innovation Policy Papers (Organisation for Economic Co-operation and Development).

Okano, H., Miyawaki, A., and Kasai, K. (2015). Brain/MINDS: brain-mapping project in Japan. Philos. Trans. R. Soc. Lond. B Biol. Sci. *370*, https://doi.org/10.1098/rstb.2014.0310.

Okano, H., Sasaki, E., Yamamori, T., Iriki, A., Shimogori, T., Yamaguchi, Y., Kasai, K., and Miyawaki, A. (2016). Brain/MINDS: a Japanese national brain project for marmoset neuroscience. Neuron *92*, 582–590.

Orsborn, A.L., Moorman, H.G., Overduin, S.A., Shanechi, M.M., Dimitrov, D.F., and Carmena, J.M. (2014). Closed-loop decoder adaptation shapes neural plasticity for skillful neuroprosthetic control. Neuron *82*, 1380–1393.

Osawa, H., Ema, A., Hattori, H., Akiya, N., Kanzaki, N., Kubo, A., Koyama, T., and Ichise, R. (2017). Analysis of robot hotel: reconstruction of works with robots. Proceedings of 26th IEEE Conference.

Pankevich, D.E., Altevogt, B.M., Dunlop, J., Gage, F.H., and Hyman, S.E. (2014). Improving and accelerating drug development for nervous system disorders. Neuron *84*, 546–553.

Papadopoulos, C., Foster, J., and Caldwell, K. (2013). 'Individualism-collectivism' as an explanatory device for mental illness stigma. Community Ment. Health J. *49*, 270–280.

PCSBI (2014). Integrated approaches for neuroscience, ethics, and society. Gray Matters (Presidential Commission for the Study of Bioethical Issues).

PCSBI (2015). Topics at the intersection of neuroscience, ethics, and society. Gray Matters (Presidential Commission for the Study of Bioethical Issues).

Pescosolido, B.A., Martin, J.K., Long, J.S., Medina, T.R., Phelan, J.C., and Link, B.G. (2010). "A disease like any other"? A decade of change in public reactions to schizophrenia, depression, and alcohol dependence. Am. J. Psychiatry *167*, 1321–1330.

Poo, M.M., Du, J.L., Ip, N.Y., Xiong, Z.Q., Xu, B., and Tan, T. (2016). China Brain Project: basic neuroscience, brain diseases, and brain-inspired computing. Neuron *92*, 591–596.

Racine, E. (2010). Pragmatic Neuroethics: Improving Treatment and Understanding of the Mind-Brain (MIT Press).

Richards, L.J., and Committee, A.B.A.S.; Australian Brain Alliance Steering Committee. Electronic address: richards@uq.edu.au; Australian Brain Alliance Steering Committee (2016). Australian Brain Alliance. Neuron *92*, 597–600.

Riggall, K., Forlini, C., Carter, A., Hall, W., Weier, M., Partridge, B., and Meinzer, M. (2015). Researchers' perspectives on scientific and ethical issues with transcranial direct current stimulation: An international survey. Sci. Rep. *5*, 10618.

Rose, N. (2014). The Human Brain Project: social and ethical challenges. Neuron *82*, 1212–1215.

Rose, N., Salles, A., Domingo-Ferrer, J., and Spranger, T. (2016). In Data Protection and Privacy, B. Stahl, ed. (Human Brain Project).

Roy, D. (2012). Neuroethics, gender and the response to difference. Neuroethics *5*, 217–230.

Sahakian, B.J., and Morein-Zamir, S. (2009). Neuroscientists need neuroethics teaching. Science *325*, 147.

Sakura, O. (2012). A view from the Far East: neuroethics in Japan, Taiwan, and South Korea. East Asian science, technology, and society. Int. J. *6*, 297–301.

Salles, A., and Evers, K. (2017). Social neuroscience and neuroethics: a fruitful synergy. In Neuroscience and Social Science: The Missing Link, A. Ibáñez, L. Sedeño, and A.M. García, eds. (Cham: Springer International Publishing), pp. 531–546.

Salles, A., Evers, K., and Farisco, M. (2018). Neuroethics and philosophy in responsible research and innovation: the case of the human brain project. Neuroethics. https://doi.org/10.1007/s12152-018-9372-9.

Sarrett, J.C., and Rommelfanger, K.S. (2015). Commentary: attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism. Front. Public Health *3*, 272.

Schelle, K.J., Faulmüller, N., Caviola, L., and Hewstone, M. (2014). Attitudes toward pharmacological cognitive enhancement-a review. Front. Syst. Neurosci. *8*, 53.

Song, I., and Shin, J.Y. (2016). Prescribing patterns for attention deficit hyperactivity disorder medications among children and adolescents in Korea, 2007-2011. Epidemiol. Health *38*, e2016045.

Stevenson, S., Beattie, B.L., Bruce, L., and Illes, J. (2016). When culture informs neuroscience: considerations for community-based neurogenetics research and clinical care in a First Nation community with early onset familial Alzheimer disease. In The Oxford Handbook of Cultural Neuroscience, J.Y. Chiao, S.-C. Li, R. Seligman, and R. Turner, eds. (Oxford University Press), pp. 171–182.

Sugiyama, M., Deguchi, H., Ema, A., Kishimoto, A., Mori, J., Shiroyama, H., and Scholz, R.W. (2017). Unintended Side Effects of Digital Transition: Perspectives of Japanese Experts (Sustainability), p. 9.

Swanson, P.L. (2011). Brain Science and Kokoro (Nanzan Institute for Religion and Culture).

Tai, M.C., and Lin, C.S. (2001). Developing a culturally relevant bioethics for Asian people. J. Med. Ethics *27*, 51–54.

Vidal, F. (2009). Brainhood, anthropological figure of modernity. Hist. Human Sci. *22*, 5–36.

Wexler, A. (2015). A pragmatic analysis of the regulation of consumer transcranial direct current stimulation (TDCS) devices in the United States. J. Law Biosci. *2*, 669–696.

Whitman, J.Q. (2004). The Two Western Cultures of Privacy: Dignity versus Liberty, Volume 113 (Yale Law).

Wiener, J.B., and Roger, M.D. (2002). Comparing precaution in the United States and Europe. J. Risk Res. *5*, 317–349.

Wu, K.C.-C. (2015). Public Opinions on Legal Agency Determination in Taiwan: Does Cultural Value and Neuroscience Matter? (International Neuroethics Society).

Wu, K.C.-C. (2016). Cognitive enhancement: a Confucian perspective from Taiwan. In Cognitive Enhancement. In Ethical and Policy Implications in International Perspectives, F. Jotterand and V. D'ubljevic, eds. (Oxford University Press), pp. 111–130.

Yan, X.-X., Ma, C., Bao, A.-M., Wang, X.-M., and Gai, W.-P. (2015). Brain banking as a cornerstone of neuroscience in China. Lancet Neurol. *14*, 136.

Yang, Q., and Miller, G. (2015). East-West differences in perception of brain death. Review of history, current understandings, and directions for future research. J. Bioeth. Inq. *12*, 211–225.

Yu, N. (2009). The Chinese Heart in a Cognitive Perspective*Volume 12* (Mouton de Gruyter).

Yuste, R., and Bargmann, C. (2017). Toward a Global BRAIN Initiative. Cell *168*, 956–959.

Yuste, R., Goering, S., Arcas, B.A.Y., Bi, G., Carmena, J.M., Carter, A., Fins, J.J., Friesen, P., Gallant, J., Huggins, J.E., et al. (2017). Four ethical priorities for neurotechnologies and AI. Nature *551*, 159–163.